10/056,347

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      (FILE 'HOME' ENTERED AT 07:33:37 ON 28 JUN 2004)

      FILE 'REGISTRY' ENTERED AT 07:33:49 ON 28 JUN 2004
                E (MELOXICAM)/CN
                E MELOXICAM/CN
L1              1 S E3
L2              1 S E5
L3            576 S E1 OR SE2
L4              2 S E3 OR E5
L5              0 S (76-42-6)/CN
L6              0 S 76-42-6/CN
L7              1 S 76-42-6/RN
L8              1 S L7
                E (MORPHINE)/CN
                E MORPHINE/CN
L9              1 S E3

      FILE 'CAPLUS' ENTERED AT 07:37:43 ON 28 JUN 2004
L10            10 S L4 AND L7
L11            10 S L4 AND L8
L12             0 S L11 NOT L10
L13             2 S L4 AND (OPIAT? OR OPIOD?)
L14            12 S L4 AND (OPIAT? OR OPIOID?)
L15             9 S L14 NOT L11
L16           458 S L9 AND SYNERG?
L17            14 S L1 AND SYNERG?
L18            38 S L1 AND (OPIAT? OR OPIOID? OR MORPHIN? OR OXYCOD?)
L19           322 S L1 AND (NSAID? OR ACETAMIN? OR ASPIRIN? OR IBUPROFEN?)
L20             7 S L19 AND SYNERG?
L21           315 S L19 NOT L20
L22            85 S L21 AND (PAIN? OR ANALGES?)

      FILE 'STNGUIDE' ENTERED AT 07:49:40 ON 28 JUN 2004

      FILE 'CAPLUS' ENTERED AT 07:50:23 ON 28 JUN 2004

      FILE 'STNGUIDE' ENTERED AT 07:50:24 ON 28 JUN 2004

      FILE 'CAPLUS' ENTERED AT 07:50:45 ON 28 JUN 2004

      FILE 'STNGUIDE' ENTERED AT 07:50:45 ON 28 JUN 2004

      FILE 'CAPLUS' ENTERED AT 07:50:55 ON 28 JUN 2004

      FILE 'STNGUIDE' ENTERED AT 07:58:43 ON 28 JUN 2004

      FILE 'CAPLUS' ENTERED AT 07:59:08 ON 28 JUN 2004

      FILE 'STNGUIDE' ENTERED AT 07:59:13 ON 28 JUN 2004

      FILE 'CAPLUS' ENTERED AT 07:59:33 ON 28 JUN 2004

      FILE 'STNGUIDE' ENTERED AT 07:59:41 ON 28 JUN 2004

      FILE 'CAPLUS' ENTERED AT 08:00:01 ON 28 JUN 2004

      FILE 'STNGUIDE' ENTERED AT 08:00:08 ON 28 JUN 2004

      FILE 'CAPLUS' ENTERED AT 08:00:30 ON 28 JUN 2004
L23            30 S L22 AND IBUPROFEN?

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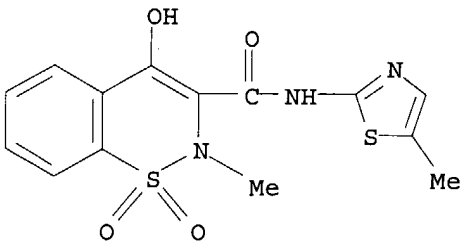
L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 71125-38-7 REGISTRY
CN 2H-1,2-Benzothiazine-3-carboxamide, 4-hydroxy-2-methyl-N-(5-methyl-2-thiazolyl)-, 1,1-dioxide (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Meloxicam**
CN Metacam
CN Mobec
CN Mobic
CN Mobicox
CN Movalis
CN UH-AC 62XX
FS 3D CONCORD
DR 133687-22-6
MF C14 H13 N3 O4 S2
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: WHO
DT.CA CAplus document type: Book; Conference; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PRP (Properties); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

613 REFERENCES IN FILE CA (1907 TO DATE)
19 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
615 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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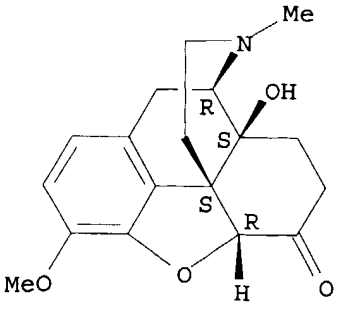
L8 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **76-42-6** REGISTRY
CN Morphinan-6-one, 4,5-epoxy-14-hydroxy-3-methoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Codeinone, 7,8-dihydro-14-hydroxy- (6CI, 7CI)
CN Morphinan-6-one, 4,5α-epoxy-14-hydroxy-3-methoxy-17-methyl- (8CI)
OTHER NAMES:
CN (-)-Oxycodone
CN 14-Hydroxydihydrocodeinone
CN 3-O-(Methyl)oxymorphone
CN 6-Oxo-14-hydroxy-7,8-dihydrocodeine
CN 7,8-Dihydro-14-hydroxycodeinone
CN Dihydro-14-hydroxycodeinone
CN Dihydrohydroxycodeinone
CN Dihydrone
CN NSC 19043
CN Oxanest
CN Oxicon
CN Oxycodeinone
CN Oxycodone
CN Oxymorphone 3-methyl ether
FS STEREOSEARCH
MF C18 H21 N O4
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PROMT, PROUSDDR, PS, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study)

Absolute stereochemistry.



L10 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
2003:971836 Document No. 140:23256 Combination therapy for treatment of amyotrophic lateral sclerosis (ALS) with cyclooxygenase-2 (COX 2) inhibitor(s) and a second drug. Isakson, Peter C. (Pharmacia Corporation, USA). PCT Int. Appl. WO 2003101380 A2 20031211, 358 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US14547 20030528. PRIORITY: US 2002-PV384104 20020531; US 2003-444071 20030523.

L10 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
2003:747138 Document No. 139:392238 Toxicological Screening with Formula-Based Metabolite Identification by Liquid Chromatography/Time-of-Flight Mass Spectrometry. Pelander, Anna; Ojanperae, Ilkka; Laks, Suvi; Rasanen, Ilpo; Vuori, Erkki (Department of Forensic Medicine, University of Helsinki, FIN-00014, Finland). Analytical Chemistry, 75(21), 5710-5718 (English) 2003. CODEN: ANCHAM. ISSN: 0003-2700. Publisher: American Chemical Society.

L10 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
2003:737369 Document No. 139:255368 Prokinetic agents for treating gastric hypomotility and related disorders. Watson, John W.; Andrews, Paul L. R.; Woods, Anthony J. (USA). U.S. Pat. Appl. Publ. US 2003176421 A1 20030918, 57 pp. (English). CODEN: USXXCO. APPLICATION: US 1999-476253 19991230.

L10 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
2001:885732 Document No. 136:11205 Combinations of an endothelin receptor antagonist and an antiepileptic compound having analgesic activity. Dooley, David James (Warner-Lambert Company, USA). PCT Int. Appl. WO 2001091736 A2 20011206, 120 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US14793 20010508. PRIORITY: US 2000-PV208259 20000531.

L10 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
2001:137173 Document No. 134:178396 Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction. Del Soldato, Piero (Nicox S.A., Fr.). PCT Int. Appl. WO 2001012584 A2 20010222, 94 pp. DESIGNATED STATES: W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-EP7225 20000727. PRIORITY: IT 1999-MI1817 19990812.

L10 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
2000:875749 Document No. 134:33001 Alkali metal and alkaline-earth metal salts of acetaminophen. Ohannesian, Lena A.; Nadig, David; Higgins, John D., III; Rey, Max; Martellucci, Stephen A. (McNeil-PPC, Inc., USA). U.S.

US 6160020 A 20001212, 10 pp., Cont.-in-part of U.S. Ser. No. 987,210, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1998-100284 19980619. PRIORITY: US 1996-771176 19961220; US 1997-987210 19971209.

L10 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
2000:742057 Document No. 133:309791 Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction. Del Soldato, Piero (Nicox S.A., Fr.). PCT Int. Appl. WO 2000061541 A2 20001019, 140 pp. DESIGNATED STATES: W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DM, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-EP3239 20000411. PRIORITY: IT 1999-MI752 19990413.

L10 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
2000:742053 Document No. 133:310142 Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction. Del Soldato, Piero (Nicox S.A., Fr.). PCT Int. Appl. WO 2000061537 A2 20001019, 159 pp. DESIGNATED STATES: W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DM, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-EP3234 20000411. PRIORITY: IT 1999-MI753 19990413.

L10 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
1999:819235 Document No. 132:54898 Pharmaceutical composition containing a salt of acetaminophen and at least one other active ingredient. Ohannesian, Lena A.; Nadig, David; Higgins, John D., III; Rey, Max; Martellucci, Stephen A. (Mcneil-PPC, Inc., USA). PCT Int. Appl. WO 9966919 A1 19991229, 31 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US13064 19990609. PRIORITY: US 1998-100284 19980619.

L10 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
1999:215565 Document No. 130:247052 Synergistic analgesic combination of opioid analgesic and cyclooxygenase-2 inhibitor. Burch, Ronald M.; Goldenheim, Paul D.; Sackler, Richard S. (Euro-Celtique, S.A., Luxembourg). PCT Int. Appl. WO 9913799 A1 19990325, 55 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US19516 19980917. PRIORITY: US 1997-59195 19970917.

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L20 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:243276 CAPLUS
DN 126:258748
ED Entered STN: 14 Apr 1997
TI A comparison between the effects of meloxicam and other **NSAIDs** on the production of oxyradicals by human polymorphonuclear leukocytes
AU Rainsford, K.D.; Ginsburg, I.; Gadd, S.J.
CS Division of Biomedical Sciences and Health Research Institute, Sheffield Hallam University, Sheffield, S1 1WB, UK
SO Inflammopharmacology (1997), 5(1), 9-19
CODEN: IAOAES; ISSN: 0925-4692
PB Kluwer
DT Journal
LA English
CC 1-7 (Pharmacology)
AB Some non-steroidal anti-inflammatory drugs (**NSAIDs**) inhibit the production or actions of oxygen radicals generated by polymorphonuclear leukocytes (PMNs); this mechanism may contribute towards their anti-inflammatory activity. In the present study, the effects of a new enolcarboxamide **NSAID**, meloxicam, on oxyradical production by human PMNs exposed to various stimuli in vitro were compared with those of other standard **NSAIDs**. The various stimuli employed were intended to mimic the likely **synergies** which occur with cytokines and bacterial production (e.g. f-met-leu-phe (fMLP) peptide) in inflamed tissues and to give an insight into the site and mechanism of action of meloxicam and related drugs on the cellular processes involved in oxyradical generation. The results show that meloxicam is a potent inhibitor of oxyradical production at drug concns. comparable with those encountered during therapy. Its mechanism of action appears similar to that of other enolcarboxamides and, while relatively complex, involves effects which are stimulus dependent and myeloperoxidase sensitive. They probably do not involve inhibition of fMLP-Gi protein receptor activation but may involve tumor necrosis factor-α post-receptor activation. Enolcarboxamides have variable effects on phorbol myristate acetate-protein kinase C3-mediated oxyradical production
ST meloxicam enolcarboxamide **NSAID** oxyradical polymorphonuclear leukocyte; antiinflammatory meloxicam **NSAID** leukocyte peroxide radical
IT Anti-inflammatory agents
Polymorphonuclear leukocyte
(meloxicam vs. other enolcarboxamide **NSAIDs** effects on oxyradicals production by human polymorphonuclear leukocytes)
IT Anti-inflammatory agents
(nonsteroidal; meloxicam vs. other enolcarboxamide **NSAIDs** effects on oxyradicals production by human polymorphonuclear leukocytes)
IT Radicals, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(oxy-; meloxicam vs. other enolcarboxamide **NSAIDs** effects on oxyradicals production by human polymorphonuclear leukocytes)
IT 34042-85-8, Sudoxicam 34552-84-6, Isoxicam 36322-90-4, Piroxicam 59804-37-4, Tenoxicam **71125-38-7**, Meloxicam
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(meloxicam vs. other enolcarboxamide **NSAIDs** effects on oxyradicals production by human polymorphonuclear leukocytes)
IT 11062-77-4, Superoxide 14915-07-2, Peroxide
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(meloxicam vs. other enolcarboxamide **NSAIDs** effects on oxyradicals production by human polymorphonuclear leukocytes)

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L22 ANSWER 66 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
1998:680323 Document No. 130:75932 Gastrointestinal tolerability of meloxicam compared to diclofenac in osteoarthritis patients.. Hawkey, C.; Kahan, A.; Steinbruck, K.; Alegre, C.; Baumelou, E.; Begaud, B.; Dequeker, J.; Isomaki, H.; Littlejohn, G.; Mau, J.; Papazoglou, S. (Queen's Medical Centre, University Hospital, Nottingham, NG7 2UH, UK). British Journal of Rheumatology, 37(9), 937-945 (English) 1998. CODEN: BJRHDF. ISSN: 0263-7103. Publisher: Oxford University Press.

AB Although widely used, non-steroidal anti-inflammatory drugs (**NSAIDs**) are associated with a high incidence of gastrointestinal (GI) side-effects. Inhibition of the cyclooxygenase (COX) enzyme is the basis for both the efficacy and toxicity of **NSAIDs**. The discovery of two COX isoforms, constitutive COX-1 and inducible COX-2, has led to the hypothesis that selective inhibition of COX-2 will minimize the potential for GI toxicity without compromising efficacy. The Meloxicam Large-scale International Study Safety Assessment (MELISSA) trial reported here was therefore set up to investigate the tolerability of meloxicam, a preferential inhibitor of COX-2, compared to diclofenac. MELISSA was a large-scale, double-blind, randomized, international, prospective trial, conducted over 28 days in patients with symptomatic osteoarthritis. Patients received either meloxicam 7.5 mg or diclofenac 100 mg slow release, the recommended doses for the treatment of osteoarthritis. Evaluation of the profile of adverse events was the main aim of the trial, together with assessment of efficacy. A total of 9323 patients received treatment (4635 and 4688 in the meloxicam and diclofenac groups, resp.). Significantly fewer adverse events were reported by patients receiving meloxicam. This was attributable to fewer GI adverse events (13%) compared to diclofenac (19%; $P < 0.001$). Of the most common GI adverse events, there was significantly less dyspepsia ($P < 0.001$), nausea and vomiting ($P < 0.05$), abdominal **pain** ($P < 0.001$) and diarrhea ($P < 0.001$) with meloxicam compared to diclofenac. Five patients on meloxicam experienced a perforation, ulcer or bleed vs seven on diclofenac (not significant). No endoscopically verified ulcer complication was detected in the meloxicam group compared to four with diclofenac. There were five patient days of hospitalization in patients on meloxicam compared to 121 with diclofenac. Adverse events caused withdrawal from the study in 254 patients receiving meloxicam (5.48%) compared to 373 (7.96%) on diclofenac ($P < 0.001$). These differences were attributable to differences in reported GI adverse events (3.02% on meloxicam vs 6.14% on diclofenac; $P < 0.001$). Differences in efficacy, as assessed by visual analog scales, consistently favored diclofenac. In all instances, 95% confidence intervals did not cross zero, suggesting a statistically significant effect. However, differences were small (4.5-9.0% difference) and did not reach pre-determined levels of clin. significance. Nevertheless, significantly more patients discontinued meloxicam because of lack of efficacy (80 out of 4635 vs 49 out of 4688; $P < 0.01$). The MELISSA trial confirms earlier studies suggesting that meloxicam has a significantly improved GI tolerability profile in comparison with other **NSAIDs** , including diclofenac. These results may in part reflect the preferential COX-2 selectivity of meloxicam, although the dose and other aspects of tolerability may be important. These results may provide support for the hypothesis that selective inhibition of COX-2 relative to COX-1 might be an effective approach towards improved **NSAID** therapy.

L22 ANSWER 67 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
1998:234258 Document No. 128:303963 Central antinociceptive effects of meloxicam on rat spinal cord in vitro. Lopez-Garcia, Jose-Antonio; Laird, Jennifer M. A. (Department of Physiology, School of Medicine, University of Alcala, Alcala de Henares, Madrid, E-28871, Spain). NeuroReport, 9(4), 647-651 (English) 1998. CODEN: NERPEZ. ISSN: 0959-4965. Publisher: Rapid Science Ltd..

AB Non-steroidal anti-inflammatory drugs inhibit constitutive (COX-1) and

induced cyclooxygenase (COX-2), blocking prostaglandin production We have compared the effects on nociceptive reflexes of meloxicam, which is COX-2 selective, with indomethacin, which is non-selective, using an in vitro spinal cord preparation Cords were taken from naive rats, and from rats with carrageenan-induced hyperalgesia of one hindpaw. Reflex thresholds were lower in carrageenan prepns. Superfusion with meloxicam (10-100 μM) dose-dependently inhibited baseline reflexes and wind-up in normal and carrageenan prepns., whereas indomethacin (100-300 μM) had no effect. Thus meloxicam inhibits spinal reflexes, whereas indomethacin does not, despite its high affinity for both COX isoforms. We conclude that meloxicam has spinal antinociceptive actions which cannot be explained by the current concept of COX inhibition.

L22 ANSWER 68 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
1997:711574 Document No. 127:326200 **Analgesic** activity of the novel COX-2 preferring **NSAID**, meloxicam in mono-arthritic rats. Central and peripheral components. Laird, J. M. A.; Herrero, J. F.; De la Rubia, P. Garcia; Cervero, F. (Fac. Medicine, Univ. Alcala, Madrid, E-28871, Spain). Inflammation Research, 46(6), 203-210 (English) 1997. CODEN: INREFB. ISSN: 1023-3830. Publisher: Birkhaeuser.
AB The characteristics and site of the **analgesic** action of meloxicam was studied on adult female rats. Monoarthritis was induced (for behavioral studies) by injection of complete Freund's adjuvant into the ankle. Meloxicam was given for 5 days (0.1-4 mg/kg/ day i.p.). Inflammation of the knee or paw (for electrophysiol.) was induced with carrageenan. Meloxicam was given i.v. (4-64 mg/kg). Rats were tested daily for joint hyperalgesia, and hindlimb posture (behavior). At post-mortem, joint stiffness, edema, and gastric lesions were assessed. In anesthetized rats, nociceptive reflex responses to stimulation of the paw were compared (electrophysiol.). Meloxicam reduced swelling and stiffness of the inflamed joint, joint hyperalgesia (ID50 = 0.4 mg/kg/ day) and spontaneous **pain**-related behavior. It also inhibited peripherally mediated reflex responses to stimulation of inflamed tissue (ID50 = 7.6 mg/kg i.v.) without affecting centrally mediated reflexes. Systemic meloxicam produces **analgesia** largely via peripheral mechanisms. The rapidity of its actions indicates a direct effect on sensitized nociceptors.

L22 ANSWER 69 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
1997:472429 Document No. 127:130328 Meloxicam: selective COX-2 inhibition in clinical practice. Furst, Daniel E. (Arthritis Clinical Research Unit, Virginia Mason Research Center, Seattle, WA, 98101, USA). Seminars in Arthritis and Rheumatism, 26(6, Suppl. 1, Meloxicam: Translating Selective COX-2 Inhibition into Clinical Benefit), 21-27 (English) 1997. CODEN: SAHRBF. ISSN: 0049-0172. Publisher: Saunders.
AB A review with 24 refs. Nonsteroidal antiinflammatory drugs (**NSAIDs**) exert their actions by inhibiting cyclooxygenase (COX). It has recently been postulated that **NSAIDs**' antiinflammatory efficacy arises from inhibition of the COX-2 isoform of cyclooxygenase, whereas inhibition of the COX-1 isoform produces the troublesome and sometimes serious gastric and renal side effects of **NSAIDs**. A relatively selective COX-2 inhibitor, such as meloxicam, may combine antiinflammatory efficacy with improved tolerability. In volunteers, indomethacin 75 mg, but not meloxicam 7.5 mg, inhibited renal prostaglandin E2 excretion and platelet aggregation (COX-1 mediated effects). Double-blind, randomized trials in osteoarthritis and rheumatoid arthritis patients have shown equivalent antiinflammatory efficacy among meloxicam 7.5 mg or 15 mg and diclofenac 100 mg, naproxen 750 mg, and piroxicam 20 mg. In a double-blind, placebo-controlled trial, meloxicam (7.5 or 15 mg) caused less endoscopically detected gastrointestinal (GI) damage (Lanza scale) than piroxicam 20 mg. The MELISSA study, a double-blind, randomized, 28-day trial in over 9,000 patients showed that meloxicam 7.5 mg caused statistically less total GI toxicity, dyspepsia, abdominal **pain**, nausea and vomiting, and

diarrhea than diclofenac 100 mg, despite equivalent redns. in **pain** on movement for each treatment. A GIobal safety anal. of clin. trials, representing over 5,600 patients and comprising 170 and 1,100 patient-years of exposure for meloxicam 7.5 mg and 15 mg, resp., showed that meloxicam caused less GI toxicity and fewer peptic ulcers and GI bleeds than naproxen, diclofenac, or piroxicam. The renal safety profile and incidence of liver function abnormalities with meloxicam is equivalent to other **NSAIDs** available for clin. use. In conclusion, relatively selective COX-2 inhibition exemplified by meloxicam may offer effective symptom relief with an improved GI tolerability profile.

L22 ANSWER 70 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
1997:367669 Document No. 127:44613 Anti-inflammatory/**analgesic** effect of meloxicam. Yoshida, Masumi; Miwa, Yoji; Kano, Mayumi; Yamaguchi, Kazumasa; Shimizu, Masayoshi; Kyuki, Kohei; Ogino, Keiko; Kanai, Kozo (Nihon Biores. Inc., Hashima, 501-62, Japan). Oyo Yakuri, 53(4/5), 351-366 (Japanese) 1997. CODEN: OYYAA2. ISSN: 0300-8533. Publisher: Oyo Yakuri Kenkyukai.

AB Anti-inflammatory/**analgesic** effect of meloxicam and the duration of the effect were compared with those of piroxicam and indomethacin in rats, guinea pigs and mice. Ulcerogenic effect of meloxicam was also examined in the intestinal mucosa in rats. (1) Anti-inflammatory effects of meloxicam on all cases of acute inflammation examined, namely, carrageenin-induced paw edema, acceleration in vascular permeability and UV erythema, were almost the same as or slightly stronger than those of piroxicam or indomethacin. (2) Anti-inflammatory effect of meloxicam on adjuvant-induced arthritis, a chronic arthritis model, was almost the same as that of piroxicam or indomethacin. Meloxicam also had stronger inhibitory effect on increases in adrenal and iliac lymph node weight gain due to adjuvant-induced arthritis, than that of piroxicam or indomethacin. (3) **Analgesic** effects of meloxicam on **pain** caused by acute inflammation (examined by Randall & Selitto's method) and on writhing reaction with acetic acid were almost the same as or slightly stronger than those of piroxicam or indomethacin. (4) **Analgesic** effect of meloxicam on **pain** caused by adjuvant-induced arthritis was the same as or slightly stronger than that of piroxicam or indomethacin. (5) The anti-inflammatory effect of meloxicam on carrageenin-induced paw edema and the **analgesic** effect of meloxicam on inflammatory **pain** (examined by Randall & Selitto's method) continued longer than those of piroxicam or indomethacin. (6) Ulcerogenic effect of meloxicam on the intestinal mucosa was markedly weaker than that of piroxicam or indomethacin. (7) No interaction of a combination of meloxicam and **aspirin** was observed in the acetic acid writhing method.

L22 ANSWER 71 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
1997:316971 Document No. 127:463 Efficacy and tolerability of meloxicam versus piroxicam in patients with osteoarthritis of the hip or knee: a six-month double-blind study. Hosie, J.; Distel, M.; Bluhmki, E. (Great Western Medical, Glasgow, UK). Clinical Drug Investigation, 13(4), 175-184 (English) 1997. CODEN: CDINFR. ISSN: 1173-2563. Publisher: Adis.

AB This study compared the efficacy and tolerability of meloxicam, a new nonsteroidal anti-inflammatory drug (**NSAID**), with piroxicam in a randomized, double-blind, parallel-group trial. 455 Patients with proven osteoarthritis of the knee or hip were randomized in a ratio of 2:1 to receive meloxicam 15mg once daily (n = 306) or piroxicam 20mg once daily (n = 149) for a 6-mo period. In the evaluation of efficacy end-points (overall **pain**, **pain** on movement, joint stiffness, global efficacy and quality of life), both drug treatments were shown to be effective and comparable. The incidence and type of adverse events were similar in both groups. The most frequently reported adverse events were gastro-intestinal disorders, reported in 24.2% of meloxicam-treated patients and 30.2% of piroxicam-treated patients. Both drugs were well tolerated. In conclusion, meloxicam is an effective and well tolerated

drug for the symptomatic treatment of osteoarthritis and is comparable in efficacy to piroxicam.

L22 ANSWER 72 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
1997:146772 Document No. 126:207293 Efficacy and safety of meloxicam in patients with rheumatoid arthritis. Lemmel, Ernst-Martin; Bolten, Wolfgang; Burgos-Vargas, Ruben; Platt, Philip; Nissilae, Martti; Sahlberg, Dick; Bjoerneboe, Olav; Baumgartner, Hubert; Valat, Jean-Paul; Franchimont, Paul; Bluhmki, Erich; Hanft, Gertraud; Distel, Manuel (Staatliches Rheumakrankenhaus, Baden-Baden, Germany). Journal of Rheumatology, 24(2), 282-290 (English) 1997. CODEN: JRHUA9. ISSN: 0315-162X. Publisher: Journal of Rheumatology Publishing Co. Ltd..
AB To evaluate the efficacy and safety of meloxicam, a new acidic enolic nonsteroidal anti-inflammatory drug, as doses of 7.5 and 15 mg once daily in patients with rheumatoid arthritis (RA). Meloxicam 15 and 7.5 mg daily was administered for 21 days in this double blind, randomized, placebo controlled study. 159 Patients received meloxicam 7.5 mg, 162 received meloxicam 15 mg, and 147 received placebo. Meloxicam 15 mg once daily was significantly superior ($p < 0.05$) to placebo in 3 of the 4 primary endpoints (disease activity assessed by the investigator, disease activity assessed by the patient, and reduction of the number of tender/**painful** joints). No difference was observed regarding number of swollen joints. The difference between meloxicam 7.5 mg once daily and placebo reached statistical significance in 2 of the 4 primary endpoints: disease activity assessed by the patient and number of tender/**painful** joints. A statistically significant difference between meloxicam 15 mg and 7.5 mg was not observed for any primary endpoint. The rating of global tolerance by investigators and patients at the end of the study was similar in the 3 treatment groups, indicating that meloxicam and placebo were generally similarly well tolerated. However, there was a slightly higher incidence of gastrointestinal (GI) disturbances reported by patients receiving meloxicam 15 mg. GI adverse events were reported by 11, 11, and 16% of patients in the placebo, meloxicam 7.5 mg, and meloxicam 15 mg groups, resp. None were serious. Meloxicam in daily doses of 7.5 and 15 mg is effective in treating the signs and symptoms of RA.

L22 ANSWER 73 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
1996:657468 Document No. 125:316606 Safety of meloxicam: A global analysis of clinical trials. Distel, M.; Mueller, C.; Bluhmki, E.; Fries, J. (Medical Department, Boehringer Ingelheim Gmb H, Biberach, 88397, Germany). British Journal of Rheumatology, 35(Suppl. 1), 68-77 (English) 1996. CODEN: BJRHDF. ISSN: 0263-7103. Publisher: Oxford University Press.
AB Meloxicam is a new preferential cyclooxygenase-2 (COX-2) inhibitor for the treatment of rheumatic disease. This paper presents a global safety anal. of data from meloxicam clin. studies, focusing on gastrointestinal (GI) adverse events. Meloxicam 7.5 and 15 mg (n = 893 and 3282) were compared with piroxicam 20 mg (n = 906), diclofenac 100 mg slow release (n = 324) and naproxen 750-1000 mg (n = 243). With respect to all GI adverse events, meloxicam 7.5 and 15 mg were significantly better than all comparators in a pooled anal. of double-blind studies in rheumatoid arthritis (RA) and osteoarthritis (OA). When examining non-serious GI events, severe GI events, discontinuations due to GI events, dyspepsia, abdominal **pain** and upper GI events, both meloxicam doses were significantly better than comparator non-steroidal anti-inflammatory drugs (**NSAIDs**) in most cases. Where statistical significance was not demonstrated, there was generally a trend in favor of meloxicam. With respect to upper GI perforations, ulcerations and bleedings, the most serious of **NSAID**-associated side-effects, meloxicam was better tolerated than the comparators, reaching statistical significance for piroxicam and naproxen. Meloxicam's improved GI safety profile is likely to be due to its preferential inhibition of inducible COX-2 relative to constitutive COX-1.

L22 ANSWER 74 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
1996:657466 Document No. 125:316604 An open study to assess the safety and tolerability of meloxicam 15 mg in subjects with rheumatic disease and mild renal impairment. Bevis, P. J. R.; Bird, H. A.; Lapham, G. (Boehringer Ingelheim Ltd, Bracknell, RG12 8 YS, UK). British Journal of Rheumatology, 35(Suppl. 1), 56-60 (English) 1996. CODEN: BJRHDF. ISSN: 0263-7103. Publisher: Oxford University Press.
AB Meloxicam is a new non-steroidal anti-inflammatory drug (**NSAID**) which has shown potent anti-inflammatory properties but good gastrointestinal (GI) and renal tolerability. The safety and tolerability profile of orally administered meloxicam 15 mg given once daily over a 28 day treatment period in renally impaired patients with rheumatic disease is presented here. A total of 25 patients (aged 43-78 yr, mean age 70 yr) with rheumatic disease and mild renal impairment were enrolled in this multicenter, open-label study, with 22 patients completing the 28 day treatment period. The median estimated creatinine clearance and N-acetyl-β-glucosaminidase/creatinine ratios (a marker of renal tubular damage) recorded at day 14, day 28 or 4-7 days after meloxicam treatment was terminated, were not statistically significantly different from baseline values. There was no evidence of accumulation of meloxicam. Overall, meloxicam was well tolerated. The most common adverse events were GI complaints of abdominal **pain** and dyspepsia. No adverse events related to the urinary system, or increases in serum urea or potassium were recorded. The results suggest that meloxicam, 15 mg once daily, does not further compromise renal function or result in accumulation of meloxicam over this treatment period in patients with pre-existing mild renal impairment.

L22 ANSWER 75 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
1996:657463 Document No. 125:316601 Meloxicam in osteoarthritis: A 6-month, double-blind comparison with diclofenac sodium. Hosie, J.; Distel, M.; Bluhmki, E. (Great Western Medical, Kinghtswood/Glasgow, UK). British Journal of Rheumatology, 35(Suppl. 1), 39-43 (English) 1996. CODEN: BJRHDF. ISSN: 0263-7103. Publisher: Oxford University Press.
AB A multicenter, double-blind, randomized study was conducted in patients with osteoarthritis (OA) of the hip or knee in order to compare the efficacy and safety of the new cyclooxygenase-2 (COX-2) inhibitor, meloxicam, with diclofenac sodium, a conventional treatment for this condition. Three hundred and thirty-six patients were treated with oral meloxicam 7.5 mg once daily or diclofenac 100 mg slow release once daily for 6 mo. There were no significant differences between the treatment groups with respect to overall **pain**, **pain** on movement, global efficacy or quality of life scores at the end of treatment, all of which showed good levels of improvement. Sixty-six patients were withdrawn after the start of the double-blind phase due to adverse events (n = 21, meloxicam; n = 31, diclofenac) or to lack of efficacy (seven in each group). The median dose of paracetamol taken concomitantly was statistically significantly lower in the meloxicam group than in the diclofenac group (185 vs 245 mg/day; P = 0.0123) with a comparable proportion of patients taking concomitant paracetamol therapy in both groups. Both drugs were well tolerated, although severe adverse events, treatment withdrawals and clin. significant laboratory abnormalities were more common with diclofenac than with meloxicam. Thus, meloxicam 7.5 mg is a safe and effective treatment for OA of the hip and knee which demonstrates a trend towards an improved safety profile compared with diclofenac.

L22 ANSWER 76 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
1996:657462 Document No. 125:316600 A double-blind study to compare the efficacy and safety of meloxicam 15 mg with piroxicam 20 mg in patients with osteoarthritis of the hip. Linden, B.; Distel, M.; Bluhmki, E. (Eksjoe Hospital, Eksjoe, S-57581, Swed.). British Journal of Rheumatology, 35(Suppl. 1), 35-38 (English) 1996. CODEN: BJRHDF. ISSN: 0263-7103. Publisher: Oxford University Press.
AB Meloxican 15 mg once daily (n = 128) was compared with piroxicam 20 mg (n

= 127) in this 6 wk, double-blind, parallel-group, randomized, multicenter study in out-patients with symptomatic osteoarthritis (OA) of the hip. Assessments of **pain**, global efficacy and global tolerance were made on a 10 cm horizontal visual analog scale; severity of OA was evaluated by Lequesne's index. Efficacy results showed significant improvement compared with baseline, with no significant difference between meloxicam 15 mg and piroxicam 20 mg. The type and frequency of adverse events were comparable for the two drugs. The most frequent events reported were gastrointestinal (GI) disorders, occurring in 21 and 23% of meloxicam and piroxicam patients resp. The global tolerance assessment by patients at the end of treatment favored meloxicam. In conclusion, meloxicam at a dose of 15 mg/day is comparable in efficacy and safety to piroxicam 20 mg.

L22 ANSWER 77 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN

1996:657461 Document No. 125:316599 A long-term study to evaluate the safety and efficacy of meloxicam therapy in patients with rheumatoid arthritis. Huskisson, E. C.; Ghozlan, R.; Kurthen, R.; Degner, F. L.; Bluhmki, E. (St Bartholomews Hospital, London, EC1A 7BE, UK). British Journal of Rheumatology, 35(Suppl. 1), 29-34 (English) 1996. CODEN: BJRHDF. ISSN: 0263-7103. Publisher: Oxford University Press.

AB Meloxicam is a new non-steroidal anti-inflammatory drug (**NSAID**), which has a higher activity against cyclooxygenase-2 (COX-2) than against cyclooxygenase-1 (COX-1), with potentially high anti-inflammatory and **analgesic** action. This study was designed to assess the long-term safety and efficacy of meloxicam 15 mg daily. Three hundred and fifty-seven patients (aged 19-84 yr, mean 56 yr) with rheumatoid arthritis (RA) received meloxicam 15 mg orally once daily, for up to 18 mo. Sixty-six per cent of patients remained on therapy for 18 mo. Mean global efficacy, assessed by each patient on a visual analog scale (0 cm = excellent, 10 cm = useless), was 3.32 ± 3.1 cm at the last study visit (all patients included) and 2.33 ± 2.25 cm after 18 mo. Health status, general condition, morning stiffness, grip strength of right hand, Ritchie joint index, **pain** in the morning and **pain** at night all improved significantly. Efficacy was maintained throughout the study. Only 11.4% of patients discontinued prematurely due to lack of efficacy. Mean global tolerance was good. Twenty-eight per cent of patients experienced gastrointestinal (GI) adverse events, 21% musculoskeletal system disorders, 18% skin disorders and 15% respiratory disorders. Only 13.7% of patients discontinued due to adverse events. Severe GI effects, such as perforation, ulcer and bleeding, occurred in only three patients (0.8%). Withdrawals due to GI adverse events occurred in 3.9% of patients. Meloxicam 15 mg once daily was effective and compared favorably with standard **NSAIDs** regarding tolerance when administered to patients with RA over an 18 mo period.

L22 ANSWER 78 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN

1996:657460 Document No. 125:316598 A six-month double-blind trial to compare the efficacy and safety of meloxicam 7.5 mg daily and naproxen 750 mg daily in patients with rheumatoid arthritis. Wojtulewski, J. A.; Schattenkirchner, M.; Barcelo, P.; Leloet, X.; Bevis, P. J. R.; Bluhmki, E.; Distel, M. (Eastbourne District General Hospital, Eastbourne, BN21 2UD, UK). British Journal of Rheumatology, 35(Suppl. 1), 22-28 (English) 1996. CODEN: BJRHDF. ISSN: 0263-7103. Publisher: Oxford University Press.

AB Meloxicam is a new non-steroidal anti-inflammatory drug (**NSAID**) which preferentially inhibits cyclooxygenase-2 over cyclooxygenase-1. A double-blind, parallel-group trial compared meloxicam 7.5 mg once daily (n = 199) with naproxen 750 mg (n = 180) in rheumatoid arthritis. There was no significant difference between the groups regarding the primary efficacy variables (global efficacy assessment by patient and investigator, number of **painful**/tender and swollen joints) and eight of the ten secondary efficacy endpoints. Only the swollen joint severity index and the number of discontinuations due to lack of efficacy

favored naproxen 750 mg significantly over meloxicam 7.5 mg. Meloxicam was better tolerated in the gastrointestinal (GI) tract, with fewer GI adverse events in the meloxicam-treated group (30.3%) than in the naproxen-treated group (44.7%), where two patients developed ulcers. No ulcers were seen in meloxicam patients. Significantly more patients discontinued due to GI adverse events in the naproxen group. Addnl., there was a significant decrease in Hb and a significant increase in serum creatinine and urea in the naproxen group compared with the meloxicam group. In conclusion, meloxicam 7.5 mg once daily is a promising treatment in rheumatoid arthritis, with efficacy comparable to naproxen 750 mg. Meloxicam has the advantage of a significantly lower incidence of GI and renal side effects.

L22 ANSWER 79 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN

1996:657459 Document No. 125:316597 A double-blind, three-week study to compare the efficacy and safety of meloxicam 7.5 mg and meloxicam 15 mg in patients with rheumatoid arthritis. Reginster, J. Y.; Distel, M.; Bluhmki, E. (Bone and Cartilage Metabolism Research Unit, University Liege, Liege, 4020, Belg.). British Journal of Rheumatology, 35(Suppl. 1), 17-21 (English) 1996. CODEN: BJRHDF. ISSN: 0263-7103. Publisher: Oxford University Press.

AB A multicenter, double-blind, randomized study was conducted in patients with rheumatoid arthritis (RA) in order to compare the efficacy and safety of two different doses of meloxicam, a new preferential cyclooxygenase-2 (COX-2) inhibitor. Four hundred and twenty-three patients were randomized to receive once-daily oral meloxicam 7.5 mg (n = 216) or meloxicam 15 mg (n = 207) for 3 wk. The Ritchie joint index and **pain** in the morning were significantly improved vs. baseline ($P < 0.001$) in both groups. There were no significant differences between the effects of each dose with respect to these measures nor with respect to final assessment of global efficacy by the patients. However, the 15 mg dose was associated with a significantly ($P < 0.05$) better effect on morning stiffness and grip strength. No differences between the doses were observed with regard to the other secondary efficacy parameters (**pain** at night, body weight and erythrocyte sedimentation rate). Both doses of meloxicam were well tolerated. There were no differences between the doses with respect to global tolerance as assessed by the patient and the patients, "general condition". In conclusion, meloxicam at a once-daily close of either 7.5 or 15 mg is well tolerated and effective in the treatment of patients with RA.

L22 ANSWER 80 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN

1996:657457 Document No. 125:292089 Pharmacology of meloxicam, a new non-steroidal anti-inflammatory drug with an improved safety profile through preferential inhibition of COX-2. Engelhardt, G. (Department Biological Research, Dr Karl Thomae GmbH, Biberach, D-88400, Germany). British Journal of Rheumatology, 35(Suppl. 1), 4-12 (English) 1996. CODEN: BJRHDF. ISSN: 0263-7103. Publisher: Oxford University Press.

AB A review with 69 refs. is presented on key pharmacol. findings of a new non-steroidal anti-inflammatory drug (**NSAID**), meloxicam. Unlike established **NSAIDs**, meloxicam preferentially inhibits inducible COX-2 in guinea-pig peritoneal macrophages and human COX-2 in COS cells. Compared with other **NSAIDs**, meloxicam is the most potent inhibitor of prostaglandin biosynthesis in pleural and peritoneal exudate, but only a weak inhibitor in the gastric tract and kidney. Ulcerogenicity in the rat stomach is weak in relation to anti-inflammatory potency, resulting in a high therapeutic index. Meloxicam's high anti-inflammatory potency combined with good tolerability can be explained by its preferential inhibition of COX-2. In adjuvant arthritis rats, meloxicam inhibits not only paw swelling, but also bone and cartilage destruction and systemic signs of disease. It inhibits leukocyte migration, but has no effect on leukotriene B4 or C4. Meloxicam shows a long-lasting anti-inflammatory and **analgesic** effect on inflammatory **pain** and reduces pyrogen-induced fever, but has no central nervous

system effects. The pharmacokinetic profile of meloxicam in the rat is similar to that in man. Metabolites are inactive.

L22 ANSWER 81 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
1996:494787 Document No. 125:132627 The efficacy and tolerability of an 8-day administration of intravenous and oral meloxicam: a comparison with intramuscular and oral diclofenac in patients with acute lumbago. Colberg, Klaus; Hettich, Marceline; Sigmund, Ralf; Degner, Frank L.; et al. (Bad Segeberg, D-23795, Germany). Current Medical Research and Opinion, 13(7), 363-377 (English) 1996. CODEN: CMROCX. ISSN: 0300-7995. Publisher: Clayton-Wray Publications Ltd.

AB In this controlled, randomized, parallel and open multi-center study, the efficacy and tolerability of a regimen comprising i.v. meloxicam followed by oral therapy was compared with a standard regimen of i.m. diclofenac followed by oral dosing in patients with acute lumbago. Of a total of 183 patients, 92 were randomized to receive meloxicam 15 mg i.v. on day 1 followed by 7 days oral treatment with one 15 mg tablet daily, and 91 patients received diclofenac 75 mg i.m. on day 1 followed by 6 days treatment with one 100 mg slow release tablet daily. **Pain** on movement and limitation of activities were assessed by patients and physicians using questionnaires. Meloxicam i.v. demonstrated a significantly faster median time of onset of **analgesic** action (30 min), compared with diclofenac i.m. (60 min). The reduction in **pain** during movement 30 min after injection was also significantly in favor of meloxicam. Assessments of global efficacy indicated that meloxicam was significantly better than diclofenac as rated by investigators and patients. Moreover, the rating of investigators and patients for local and global tolerance was significantly in flavor of meloxicam and improvements in the quality of life were almost significant. Fewer adverse events, particularly of a gastrointestinal (GI) nature, occurred in the meloxicam group compared with the diclofenac group. This study therefore demonstrates that meloxicam 15 mg i.v. followed by oral therapy is both efficacious and well tolerated in the treatment of acute lumbago, and compares favorably with the standard **NSAID**, in this indication.

L22 ANSWER 82 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
1996:424644 Document No. 125:104588 General pharmacology of meloxicam. Part II: Effects on blood pressure, blood flow, heart rate, ECG, respiratory minute volume and interactions with paracetamol, pirenzepine, chlorthalidone, phenprocoumon and tolbutamide. Engelhardt, G.; Homma, D.; Schlegel, K.; Schnitzler, Chr.; Utzmann, R. (Department of Pharmacologic Research, Dr. Karl Thomae GMBH, Biberach/Riss, 88397, Germany). General Pharmacology, 27(4), 679-688 (English) 1996. CODEN: GEPHDP. ISSN: 0306-3623. Publisher: Elsevier.

AB The pharmacodynamic properties of meloxicam, a new nonsteroidal antiinflammatory drug (**NSAID**), that go beyond those typical of an **NSAID** were examined The extent to which meloxicam shows **NSAID**-like interactions with paracetamol, pirenzepine, chlorthalidone, phenprocoumon and tolbutamide was also investigated. In the dose range studied, meloxicam had no influence on the blood pressure of the unanesthetized rat, blood flow, heart rate, ECG and respiratory minute volume of the anesthetized cat or on the blood pressure, heart rate and respiratory minute volume of the anesthetized dog. The acute toxicity level of meloxicam after oral and parenteral administration to the rat and mouse proved considerably lower than that of indomethacin. Meloxicam showed excellent tissue tolerability following parenteral administration. The effects against inflammatory **pain** and acute antiexudative effects of meloxicam were enhanced by simultaneous low doses of paracetamol. Pirenzepine showed an antagonistic effect on the ulcerogenicity of meloxicam in the rat stomach. The diuretic effect of chlorthalidone in the rat was not influenced by high doses of meloxicam. The effect of phenprocoumon in the rat was enhanced by high doses of meloxicam. However, the hypoglycemic effect of tolbutamide in the rabbit

was not influenced by meloxicam.

L22 ANSWER 83 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
1996:258953 Document No. 124:306898 Global analysis of gastrointestinal safety of a new **NSAID** [nonsteroidal anti-inflammatory drug], meloxicam. Distel, M.; Mueller, C.; Bluhmki, E. (Medical Department, Dr Karl Thomas GmbH, Biberach, Germany). Inflammopharmacology, 4(1), 71-81 (English) 1996. CODEN: IAOAES. ISSN: 0925-4692. Publisher: Kluwer.
AB This paper presents a safety anal. of data from meloxicam clin. studies, focusing on gastrointestinal (GI) adverse events. Meloxicam doses of 7.5 mg and 15 mg were compared with piroxicam at 20 mg, slow-release diclofenac at 100 mg, and naproxen at 750-1000 mg. With respect to all GI adverse events, both doses of meloxicam were superior to all the other drugs in a pooled anal. of double-blind studies in rheumatoid arthritis and osteoarthritis. With reference to nonserious GI events, severe GI events, discontinuations due to GI events, dyspepsia, abdominal **pain** and upper GI events, both meloxicam doses were superior to the other **NSAIDs** in most cases. Where statistical significance was not demonstrated, there was generally a clear trend in favor of meloxicam. With respect to upper GI perforations, ulcerations and bleedings, the most serious **NSAID**-associated side-effects, meloxicam was better tolerated than the other drugs, the data reaching statistical significance for piroxicam and naproxen. Meloxicam's greater GI safety profile is likely due to its preferential inhibition of inducible cyclo-oxygenase-2 relative to constitutive cyclo-oxygenase-1.

L22 ANSWER 84 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
1996:239185 Document No. 124:332258 A comparison of the local tolerability, safety and efficacy of meloxicam and piroxicam suppositories in patients with osteoarthritis: A single-blind, randomized, multicenter study. Carrabba, M.; Paresce, E.; Angelini, M.; Galanti, A.; Marini, M. G.; Cigarini, P. (Osteoarthritis and Extra-articular Rheumatism Unit, Hospital G. Pini, Milan, Italy). Current Medical Research and Opinion, 13(6), 343-55 (English) 1995. CODEN: CMROCX. ISSN: 0300-7995. Publisher: Clayton-Wray Publications Ltd.
AB The local tolerability, safety and efficacy of meloxicam 15 mg suppositories were compared with piroxicam 20 mg suppositories over a 3-wk period in a single-blind, randomized study in patients with osteoarthritis. Patients were randomized 2:1 to receive meloxicam (n = 216) or piroxicam (n = 109). More than 90% of patients and investigators assessed local tolerability of both treatments as good or very good (primary endpoint). There was no significant difference between the groups. Global efficacy was reported by approx. 80% of patients in both groups to be good or very good. **Pain** on movement and at rest and joint mobility showed statistically significant improvements compared with baseline with both meloxicam and piroxicam; there were no statistically significant differences between treatment groups. Piroxicam and meloxicam suppositories were equally well tolerated, with no serious adverse events recorded in either treatment group. Local adverse events occurred in 11.9% of patients receiving piroxicam and 6.9% of those receiving meloxicam. Overall, gastrointestinal adverse events were the most frequent of all adverse events reported in both groups (9.2% of meloxicam-treated patients and 11.9% of piroxicam-treated patients). In both groups, about 90% of global tolerability assessments were classified, by the investigator and the patient, as either very good or good. In conclusion, meloxicam 15 mg suppositories showed excellent local tolerability accompanied by good safety and efficacy in osteoarthritis, which was comparable to that of an established non-steroidal anti-inflammatory drug (**NSAID**) administered by the rectal route, and to that previously observed with oral formulations of meloxicam 15 mg.

L22 ANSWER 85 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
1995:906352 Document No. 123:329575 Anti-inflammatory, **analgesic**, antipyretic and related properties of meloxicam, a new non-steroidal

anti-inflammatory agent with favorable gastrointestinal tolerance.
Engelhardt, G.; Homma, D.; Schlegel, K.; Utzmann, R.; Schnitzler, C. (Dep. Pharmacologic Res., Biberach/Riss, D-88397, Germany). Inflammation Research, 44(10), 423-33 (English) 1995. CODEN: INREFB. ISSN: 1023-3830. Publisher: Birkhaeuser.

AB The anti-inflammatory, **analgesic** and antipyretic properties of the new non-steroidal anti-inflammatory agent, meloxicam, were investigated in a variety of animal models and compared with the properties of piroxicam, diclofenac, indomethacin and several other **NSAIDs**. With respect to the total effect of a single oral dose, the anti-exudative effect of meloxicam on carrageenan-induced edema in the rat exceeded that of all the **NSAIDs** included in the comparison. Addnl., meloxicam showed the greatest potency of all the compds. examined with respect to adjuvant-induced arthritis in the rat, the granuloma pouch model and the cotton pellet test in the rat. Unlike indomethacin, in the carrageenan pleurisy model in the rat, meloxicam caused both a dose-dependent reduction in exudate volume and also inhibition of leukocyte migration. Meloxicam showed a strong and lasting effect on inflammatory **pain** in the rat. Like other **NSAIDs**, but unlike dipyrone, meloxicam had no effect in the hot plate and tail clamp tests, which are used to identify weak central **analgesic** effects. Unlike dipyrone and like indomethacin, meloxicam had no effect in a model of visceral distention **pain**. In common with other **NSAIDs**, meloxicam had no influence on the body temperature of normothermic rats in the anti-inflammatory dose range, but did reduce yeast-induced fever in the rat in a dose-dependent manner. Like piroxicam, meloxicam had a uricosuric effect on rats treated with oxonic acid. Low-dose meloxicam inhibited both bradykinin-induced and PAF-induced bronchospasm in the guinea-pig, but had no effect on acetylcholine-induced bronchospasm. Piroxicam had greater ulcerogenic effects in the rat stomach than meloxicam. The therapeutic range of meloxicam in the rat, with regard to inhibition of adjuvant arthritis, was several times greater than that of piroxicam, indomethacin, diclofenac and naproxen.

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L22 ANSWER 78 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:657460 CAPLUS
DN 125:316598
TI A six-month double-blind trial to compare the efficacy and safety of meloxicam 7.5 mg daily and naproxen 750 mg daily in patients with rheumatoid arthritis
AU Wojtulewski, J. A.; Schattenkirchner, M.; Barcelo, P.; Leloet, X.; Bevis, P. J. R.; Bluhmki, E.; Distel, M.
CS Eastbourne District General Hospital, Eastbourne, BN21 2UD, UK
SO British Journal of Rheumatology (1996), 35(Suppl. 1), 22-28
CODEN: BJRHDF; ISSN: 0263-7103
PB Oxford University Press
DT Journal
LA English
AB Meloxicam is a new non-steroidal anti-inflammatory drug (**NSAID**) which preferentially inhibits cyclooxygenase-2 over cyclooxygenase-1. A double-blind, parallel-group trial compared meloxicam 7.5 mg once daily (n = 199) with naproxen 750 mg (n = 180) in rheumatoid arthritis. There was no significant difference between the groups regarding the primary efficacy variables (global efficacy assessment by patient and investigator, number of **painful**/tender and swollen joints) and eight of the ten secondary efficacy endpoints. Only the swollen joint severity index and the number of discontinuations due to lack of efficacy favored naproxen 750 mg significantly over meloxicam 7.5 mg. Meloxicam was better tolerated in the gastrointestinal (GI) tract, with fewer GI adverse events in the meloxicam-treated group (30.3%) than in the naproxen-treated group (44.7%), where two patients developed ulcers. No ulcers were seen in meloxicam patients. Significantly more patients discontinued due to GI adverse events in the naproxen group. Addnl., there was a significant decrease in Hb and a significant increase in serum creatinine and urea in the naproxen group compared with the meloxicam group. In conclusion, meloxicam 7.5 mg once daily is a promising treatment in rheumatoid arthritis, with efficacy comparable to naproxen 750 mg. Meloxicam has the advantage of a significantly lower incidence of GI and renal side effects.

L22 ANSWER 80 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:657457 CAPLUS
DN 125:292089
TI Pharmacology of meloxicam, a new non-steroidal anti-inflammatory drug with an improved safety profile through preferential inhibition of COX-2
AU Engelhardt, G.
CS Department Biological Research, Dr Karl Thomae GmbH, Biberach, D-88400, Germany
SO British Journal of Rheumatology (1996), 35(Suppl. 1), 4-12
CODEN: BJRHDF; ISSN: 0263-7103
PB Oxford University Press
DT Journal; General Review
LA English
AB A review with 69 refs. is presented on key pharmacol. findings of a new non-steroidal anti-inflammatory drug (**NSAID**), meloxicam. Unlike established **NSAIDs**, meloxicam preferentially inhibits inducible COX-2 in guinea-pig peritoneal macrophages and human COX-2 in COS cells. Compared with other **NSAIDs**, meloxicam is the most potent inhibitor of prostaglandin biosynthesis in pleural and peritoneal exudate, but only a weak inhibitor in the gastric tract and kidney. Ulcerogenicity in the rat stomach is weak in relation to anti-inflammatory potency, resulting in a high therapeutic index. Meloxicam's high anti-inflammatory potency combined with good tolerability can be explained by its preferential inhibition of COX-2. In adjuvant arthritis rats, meloxicam inhibits not only paw swelling, but also bone and cartilage destruction and systemic signs of disease. It inhibits leukocyte migration, but has no effect on leukotriene B4 or C4. Meloxicam shows a long-lasting

anti-inflammatory and **analgesic** effect on inflammatory **pain** and reduces pyrogen-induced fever, but has no central nervous system effects. The pharmacokinetic profile of meloxicam in the rat is similar to that in man. Metabolites are inactive.

L22 ANSWER 81 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:494787 CAPLUS
DN 125:132627
TI The efficacy and tolerability of an 8-day administration of intravenous and oral meloxicam: a comparison with intramuscular and oral diclofenac in patients with acute lumbago
AU Colberg, Klaus; Hettich, Marceline; Sigmund, Ralf; Degner, Frank L.; et al.
CS Bad Segeberg, D-23795, Germany
SO Current Medical Research and Opinion (1996), 13(7), 363-377
CODEN: CMROCX; ISSN: 0300-7995
PB Clayton-Wray Publications Ltd
DT Journal
LA English
AB In this controlled, randomized, parallel and open multi-center study, the efficacy and tolerability of a regimen comprising i.v. meloxicam followed by oral therapy was compared with a standard regimen of i.m. diclofenac followed by oral dosing in patients with acute lumbago. Of a total of 183 patients, 92 were randomized to receive meloxicam 15 mg i.v. on day 1 followed by 7 days oral treatment with one 15 mg tablet daily, and 91 patients received diclofenac 75 mg i.m. on day 1 followed by 6 days treatment with one 100 mg slow release tablet daily. **Pain** on movement and limitation of activities were assessed by patients and physicians using questionnaires. Meloxicam i.v. demonstrated a significantly faster median time of onset of **analgesic** action (30 min), compared with diclofenac i.m. (60 min). The reduction in **pain** during movement 30 min after injection was also significantly in favor of meloxicam. Assessments of global efficacy indicated that meloxicam was significantly better than diclofenac as rated by investigators and patients. Moreover, the rating of investigators and patients for local and global tolerance was significantly in flavor of meloxicam and improvements in the quality of life were almost significant. Fewer adverse events, particularly of a gastrointestinal (GI) nature, occurred in the meloxicam group compared with the diclofenac group. This study therefore demonstrates that meloxicam 15 mg i.v. followed by oral therapy is both efficacious and well tolerated in the treatment of acute lumbago, and compares favorably with the standard **NSAID**, in this indication.

L22 ANSWER 83 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:258953 CAPLUS
DN 124:306898
TI Global analysis of gastrointestinal safety of a new **NSAID** [nonsteroidal anti-inflammatory drug], meloxicam
AU Distel, M.; Mueller, C.; Bluhmki, E.
CS Medical Department, Dr Karl Thomas GmbH, Biberach, Germany
SO Inflammopharmacology (1996), 4(1), 71-81
CODEN: IAOAES; ISSN: 0925-4692
PB Kluwer
DT Journal
LA English
AB This paper presents a safety anal. of data from meloxicam clin. studies, focusing on gastrointestinal (GI) adverse events. Meloxicam doses of 7.5 mg and 15 mg were compared with piroxicam at 20 mg, slow-release diclofenac at 100 mg, and naproxen at 750-1000 mg. With respect to all GI adverse events, both doses of meloxicam were superior to all the other drugs in a pooled anal. of double-blind studies in rheumatoid arthritis and osteoarthritis. With reference to nonserious GI events, severe GI events, discontinuations due to GI events, dyspepsia, abdominal **pain** and

upper GI events, both meloxicam doses were superior to the other **NSAIDs** in most cases. Where statistical significance was not demonstrated, there was generally a clear trend in favor of meloxicam. With respect to upper GI perforations, ulcerations and bleedings, the most serious **NSAID**-associated side-effects, meloxicam was better tolerated than the other drugs, the data reaching statistical significance for piroxicam and naproxen. Meloxicam's greater GI safety profile is likely due to its preferential inhibition of inducible cyclo-oxygenase-2 relative to constitutive cyclo-oxygenase-1.

L22 ANSWER 85 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:906352 CAPLUS
DN 123:329575
TI Anti-inflammatory, **analgesic**, antipyretic and related properties of meloxicam, a new non-steroidal anti-inflammatory agent with favorable gastrointestinal tolerance
AU Engelhardt, G.; Homma, D.; Schlegel, K.; Utzmann, R.; Schnitzler, C.
CS Dep. Pharmacologic Res., Biberach/Riss, D-88397, Germany
SO Inflammation Research (1995), 44(10), 423-33
CODEN: INREFB; ISSN: 1023-3830
PB Birkhaeuser
DT Journal
LA English
AB The anti-inflammatory, **analgesic** and antipyretic properties of the new non-steroidal anti-inflammatory agent, meloxicam, were investigated in a variety of animal models and compared with the properties of piroxicam, diclofenac, indomethacin and several other **NSAIDs**. With respect to the total effect of a single oral dose, the anti-exudative effect of meloxicam on carrageenan-induced edema in the rat exceeded that of all the **NSAIDs** included in the comparison. Addnl., meloxicam showed the greatest potency of all the compds. examined with respect to adjuvant-induced arthritis in the rat, the granuloma pouch model and the cotton pellet test in the rat. Unlike indomethacin, in the carrageenan pleurisy model in the rat, meloxicam caused both a dose-dependent reduction in exudate volume and also inhibition of leukocyte migration. Meloxicam showed a strong and lasting effect on inflammatory **pain** in the rat. Like other **NSAIDs**, but unlike dipyrone, meloxicam had no effect in the hot plate and tail clamp tests, which are used to identify weak central **analgesic** effects. Unlike dipyrone and like indomethacin, meloxicam had no effect in a model of visceral distention **pain**. In common with other **NSAIDs**, meloxicam had no influence on the body temperature of normothermic rats in the anti-inflammatory dose range, but did reduce yeast-induced fever in the rat in a dose-dependent manner. Like piroxicam, meloxicam had a uricosuric effect on rats treated with oxonic acid. Low-dose meloxicam inhibited both bradykinin-induced and PAF-induced bronchospasm in the guinea-pig, but had no effect on acetylcholine-induced bronchospasm. Piroxicam had greater ulcerogenic effects in the rat stomach than meloxicam. The therapeutic range of meloxicam in the rat, with regard to inhibition of adjuvant arthritis, was several times greater than that of piroxicam, indomethacin, diclofenac and naproxen.

L22 ANSWER 73 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:657468 CAPLUS
DN 125:316606
TI Safety of meloxicam: A global analysis of clinical trials
AU Distel, M.; Mueller, C.; Bluhmki, E.; Fries, J.
CS Medical Department, Boehringer Ingelheim Gmb H, Biberach, 88397, Germany
SO British Journal of Rheumatology (1996), 35(Suppl. 1), 68-77
CODEN: BJRHDF; ISSN: 0263-7103
PB Oxford University Press
DT Journal
LA English

AB Meloxicam is a new preferential cyclooxygenase-2 (COX-2) inhibitor for the treatment of rheumatic disease. This paper presents a global safety anal. of data from meloxicam clin. studies, focusing on gastrointestinal (GI) adverse events. Meloxicam 7.5 and 15 mg (n = 893 and 3282) were compared with piroxicam 20 mg (n = 906), diclofenac 100 mg slow release (n = 324) and naproxen 750-1000 mg (n = 243). With respect to all GI adverse events, meloxicam 7.5 and 15 mg were significantly better than all comparators in a pooled anal. of double-blind studies in rheumatoid arthritis (RA) and osteoarthritis (OA). When examining non-serious GI events, severe GI events, discontinuations due to GI events, dyspepsia, abdominal **pain** and upper GI events, both meloxicam doses were significantly better than comparator non-steroidal anti-inflammatory drugs (**NSAIDs**) in most cases. Where statistical significance was not demonstrated, there was generally a trend in favor of meloxicam. With respect to upper GI perforations, ulcerations and bleedings, the most serious of **NSAID**-associated side-effects, meloxicam was better tolerated than the comparators, reaching statistical significance for piroxicam and naproxen. Meloxicam's improved GI safety profile is likely to be due to its preferential inhibition of inducible COX-2 relative to constitutive COX-1.

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